## REMARKS

Entry of the enclosed amendment to the claims is respectfully requested. As explained in more detail below, the amendment does not raise issues that would require further search and/or consideration.

**Claim objections**

The comma after the word "lymphocytes" has been deleted from Claim 12.

**Rejection under §112, second paragraph**

Claim 23 has been amended to correct the improper antecedent basis.

**Rejections under §102(e) and §103**

The claims stand rejected over June et al., U.S. Pat. No. 6,534,055. In the previous response, Applicant had argued along the lines that June et al. did not describe monoclonal antibodies which are specific for CD28 and which are capable of inducing proliferation of T lymphocytes without occupying an antigen receptor of the T lymphocytes. See, Response, dated September 22, 2005, Page 8.

The examiner dismissed this argument, stating: "... it was well known in the art at the time the invention was made that antibodies which are specific for CD28 do not occupy the antigen receptor of T lymphocytes. In light of the above interpretation, Applicant's argument that according to June et al., stimulation of CD3 and CD28 is allegedly necessary, is not found persuasive, because the argument addresses limitations not claimed." See, Office action dated November 25, 2005, Page 4.

To address this issue, the claims have now been amended to recite: "wherein said antibody specific for CD28 directly stimulates T lymphocyte proliferation, without costimulation

with CD3-specific antibodies." Support for this amendment can be found in the specification, e.g., especially at Page 20, line 27 to Page 21, line 9. The experiment described at this location shows the effect of CMY-2 (an antibody specific for CD28) on T lymphocyte cell proliferation under costimulation conditions ("Costimulation") and conditions without costimulation ("Direct stimulation"). The amendment does not raise new issues that would require further search and/or consideration since it is based on an argument previously presented in an earlier Office action, and – as indicated above – considered by the examiner. Moreover, previously presented Claim 23 recited that "said antibody which is administered consists of said antibody specific for CD28." This claim already excluded costimulation with CD3-specific antibodies. Consequently, such subject matter has already been presented for the examiner's consideration.

Evidence was also presented in previously filed Response that June et al. do not describe monoclonal antibodies which are specific for CD28 and which are capable of inducing proliferation of T lymphocytes without occupying an antigen receptor of the T lymphocytes. Applicant had cited Column 2, lines 9-27 of June et al. where it is stated:

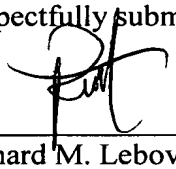
> According to the method of the invention, a population of T cells is induced to proliferate by activating the T cells and stimulating an accessory molecule on the surface of the T cells with a ligand which binds the accessory molecule. Activation of a population of T cells is accomplished by contacting the T cells with a first agent which stimulates a TCR/CD3 complex-associated signal in the T cells. Stimulation of the TCR/CD3 complex-associated signal in a T cell is accomplished either by ligation of the T cell receptor (TCR)/CD3 complex or the CD2 surface protein, or by directly stimulating receptor-coupled signaling pathways. Thus, an anti-CD3 antibody, an anti-CD2 antibody, or a protein kinase C activator in conjunction with a calcium ionophore is used to activate a population of T cells.
>
> To induce proliferation, an activated population of T cells is contacted with a second agent which stimulates an accessory molecule on the surface of the T cells. For example, a population of $CD4^+$ T cells can be stimulated to proliferate with an anti-CD28 antibody directed to the CD28 molecule on the surface of the T cells.

Thus, according to June et al., stimulation of CD3 and CD28 is necessary. The combination with Hennge et al. does not complement this deficiency since the latter disclosure is restricted to HAART.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



Richard M. Lebovitz, Reg. No. 37,067
Attorney for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

**Attorney Docket No.: ALBRE-0023**

**Date: February 23, 2006**